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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LU, FRANK WEI MIN	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 12/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/310,667	ECKER ET AL.	
	Examiner	Art Unit	
	Frank W Lu	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2004 and 30 September 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-29, 35-41, and 43-67* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-29, 35-41, and 43-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☒ The proposed drawing correction filed on *09 July 2004* is: a)☒ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

Response to Amendment

1. Applicant's response to the office action filed on July 9, 2004 and the office communication filed on September 20, 2004 has been entered. The claims pending in this application are claims 27-29, 35-41, and 43-67. Rejection and/or objection not reiterated from the previous office action are hereby withdrawn in view of the response filed on July 9, 2004.

Specification

2. The substitute specification filed on September 23, 2004 has not been entered because it does not conform to 37 CFR 1.125(b) and (c) since applicant does not provide a clean version (without markings) of the substitute specification.

Appropriate correction is required.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 27-29, 35-41, and 43-67 are rejected under 35 USC 101 because the claimed invention is directed to non-statutory subject matter.

Claims 27-29, 35-41, and 43-67 as written, do not sufficiently distinguish over naturally nucleic acids because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter.

See *Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified". See MPEP 2105.

Response to Arguments

In page 3, fourth paragraph bridging to page 4, first paragraph of applicant's remarks, applicant argues that "[T]he Office Action suggest amending the claims to recite 'isolated' or 'purified' to distinguish the claimed subject matter from the naturally occurring products. Each of the claims 27-29, 35-41, and 43-67 recite an 'oligonucleotide.' Applicants are unaware of any 'naturally occurring' oligonucleotides that comprise the same recited features as Applicants' claimed 'oligonucleotides.' Indeed, the naturally occurring nucleic acid molecules that comprise the molecular interaction sites are molecules much larger than 'oligonucleotides.'. Further, Applicants are not merely 'isolating' or 'purifying' molecules that are found in nature. Upon a showing that such claimed compounds are found in nature, Applicants will entertain the Office Action's suggestion to further amend the claims.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, although applicant argue that "[A]pplicants are unaware of any 'naturally occurring' oligonucleotides that comprise the same recited features as Applicants' claimed 'oligonucleotides.' Indeed, the naturally occurring nucleic acid molecules that comprise the molecular interaction sites are molecules much larger than 'oligonucleotides'.", since applicant does not explain why the naturally occurring nucleic acid molecules that comprise the molecular interaction sites are molecules much larger than "oligonucleotides" and applicant does not limit the claimed oligoncleotide to certain size, the naturally occurring nucleic acid

molecules read an oligoncleotide recited in claims 27-29, 35-41, and 43-67. According to 35 U.S.C. 101, in the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. Second, in fact, the examiner has shown two oligoncleotides that can read claimed oligonucleotides in previous office action (see the rejections under 35 USC 102).

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 27-29, 35-41, and 43-67 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Although the specification describes iron response element and 3' untranslated region of the histone mRNA (see specification, pages 32-38), the specification does not adequately describe that: (1) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element in claims 35-41 and 43-51; (2) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element or the 3' untranslated region of the histone mRNA in claims 52-67; and (3) the binding of said molecule to said molecular interaction site does not modulate

translation of said RNA as recited in claims 27-29. MPEP 2163.06 states that "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." In view of the embodiments adequately description in the specification, the subject application does not reasonably convey to one skilled in the art that applicant was in possession of the full scopes of products encompass in the claims at the time of the application was filled. Therefore, the written description requirement has not been satisfied.

In support of this position, attention is directed to the decision of *Vas-Cath inc. V. Mahurkar* 19 USPQ2d 1111 (CAFC, 1991):

> This court in *Wilder* (and the CCPA before it) clearly recognized, and we hereby reaffirm, that 35 U.S.C. 112, first paragraph, requires a "written description of the invention" which is separate and distinct from the enablement requirement. The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the "applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Response to Arguments

In page 5, last paragraph bridging to page 6, last paragraph of applicant's remarks, applicant argues that:(1) "[A]pplicants teach in Example 3 that the analysis shown 'describes the use of this known structure to validate the strategy and methods described herein.' Thus, Applicants used both the iron response element and the 3' untranslated region of histone RNA to validate the methods described in the specification. Applicant's validation of the methods described in the present application resulted in identifying molecular interaction sites in, for example, ornithine decarboxylase and vimentin, as well as others. Thus, Applicants clearly intended not to claim either the iron response element or the 3' untranslated region of histone

RNA, which were clearly identified in the present application to be known. Applicants also teach at, for example, page 2 of the specification that the process of RNA maturation, transport, intracellular localization and translation are rich in RNA recognition sites that provide good opportunities for drug binding. Thus, modulation of translation is but one alternative function of a molecular interaction site"; and (2) "because both the iron response element and the 3' untranslated region of histone RNA are positively recited in the present specification and are alternative elements, along with other molecular interaction sites such as ornithine decarboxylase and vimentin, they may be explicitly excluded in the claims.".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, the specification defines "Modulation" as "augmenting or diminishing RNA activity or expression" (see the specification filed on May 12, 1999, page 10, last paragraph or the specification filed on October 21, 2002, page 6, lines 12-15). Although the specification adequately describes 3' untranslated regions of histone and vimentin mRNAs and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4, the specification does not adequately describe whether a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 can be considered as a molecular interaction site since there is no evidence to show that binding of a molecule to a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 can modulate the expression of said RNAs in said organisms. Therefore, the site on 3' untranslated region of vimentin mRNA and 5' and 3' untranslated regions of mRNAs from

ornithine decarboxylase argued by applicant is not considered as the molecular interaction sites as recited in claims 27-29, 35-41, and 43-67. Second, although applicant argues that "page 2 of the specification that the process of RNA maturation, transport, intracellular localization and translation are rich in RNA recognition sites that provide good opportunities for drug binding", according to the definition of "Modulation", "RNA recognition sites good opportunities for drug binding" is not a real molecular binding site since the specification does not show that binding of a drug to its RNA recognition site can augment or diminish the RNA activity or expression. Therefore, the specification does not adequately describe that: (1) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element in claims 35-41 and 43-51; (2) an oligonucleotide comprising a molecular interaction site that is present in the RNA does not comprise the iron response element or the 3' untranslated region of the histone mRNA in claims 52-67; and (3) the binding of said molecule to said molecular interaction site does not modulate translation of said RNA as recited in claims 27-29.

6. Claims 27-29, 35-41, and 43-67 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the interim guidelines on written description published on December 21, 1999 in the Federal Register at Volume 64, Number 244, pp.71427-71440.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date

sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed". *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

The specification (for example, see page 32-44) provides adequate written descriptions for iron response element in 5' untranslated region of ferritin mRNA and in 3' untranslated region of transferrin receptor mRNA, 3' untranslated regions of histone and vimentin mRNAs, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4. However, the specification fails to adequately describe: (1) any kind of oligonucleotide comprising a molecular interaction site in RNA of a selected organism and in RNA of at least one additional organism wherein said molecular interaction site serves as a binding site for at least one molecule, wherein binding of said molecule to said molecular interaction site modulates the expression of said RNA in said selected organism and wherein said oligonucleotide does not comprise an iron response element as recited in claims 35-41 and 43-67; and (2) any kind of oligonucleotide comprising a molecular interaction site that is present in prokaryotic RNA and in at least one additional prokaryotic RNA wherein said molecular interaction site serves as a binding site for at least one molecule, wherein binding of said molecule to said molecular interaction site modulates the expression of said prokaryotic RNA and wherein the binding of said molecule to said molecular interaction site does not modulate translation of said RNA as recited in claims 27-29. The claimed inventions as a whole are not adequately described if the claims require essential or critical elements which are not adequately

described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed inventions as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998).

In this instant case, in view of the teachings in the specification, claims 35, 51, 52, and 67 are read as any kind of oligonucleotide comprising a molecular interaction site in RNA of a selected organism and in RNA of at least one additional organism wherein said molecular interaction site serves as a binding site for at least one molecule, wherein binding of said molecule to said molecular interaction site modulates the expression of said RNA in said selected organism and wherein said oligonucleotide does not comprise an iron response element. Claim 27 is read as any kind of oligonucleotide comprising a molecular interaction site that is present in prokaryotic RNA and in at least one additional prokaryotic RNA, wherein said molecular interaction site serves as a binding site for at least one molecule, wherein binding of said molecule to said molecular interaction site modulates the expression of said prokaryotic RNA and wherein the binding of said molecule to said molecular interaction site does not modulate translation of said RNA. Since independent claims 35, 51, 52, and 67 are directed to a product and are not directed to a method and it is well established that the determination of the patentability of the product is based on the product itself and is not dependent on the method for identifying the product, the method as recited in claims 35, 51, 52, and 67 is not read into claims. Since it is known in the art that iron response elements from ferritin mRNAs from different

species and human transferrin receptor have a highly conserved six-membered loop (Harrison *et al.*, Biochim. Biophys. Acta, 1275, 161-203, 1996, see page 186, Figure 12) and a sequence of 28 nucleotides within putative stem-loops in the 5'-UTR of H- and L-ferritin mRNA of human, bullfrog, chicken, rabbit and the somal ferritin of the snail *Lymnaea stagnalis* as well as in rat is highly conserved and this sequence has been demonstrated to be essential (and sufficient) for the translational response to iron (Harrison *et al.*, Biochim. Biophys. Acta, 1275, 161-203, 1996, see page 187, right column, first paragraph), iron response element is an oligonucleotide comprising a molecular interaction site in RNA of a selected organism and in RNA of at least one additional organism wherein said molecular interaction site serves as a binding site for at least one molecule (ie., iron) and wherein binding of said molecule to said molecular interaction site modulates the expression of said RNA in said selected organism. The specification defines "Modulation" as "augmenting or diminishing RNA activity or expression" (see the specification filed on May 12, 1999, page 10, last paragraph or the specification filed on October 21, 2002, page 6, lines 12-15). Although the specification adequately describes 3' untranslated regions of histone and vimentin mRNAs and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4, the specification does not adequately describe that a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 can be considered as a molecular interaction site since there is no evidence to show that binding of a molecule to a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 can modulate the expression of said RNAs in said organisms. In view of the

teachings in the specification, besides iron response element, the specification does not describe other oligonucleotides comprising a molecular interaction site as recited in claims 27-29, 35-41, and 43-67. Therefore, claims 27-29, 35-41, and 43-67 encompass numerous unknown and unidentified oligonucleotides that miss from the disclosure. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

With limited disclosure provided by the specification, the skilled artisan cannot envision all oligonucleotides recited in claims 27-29, 35-41, and 43-67 and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co.* Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only iron response element meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Response to Arguments

I. In page 7, first paragraph bridging to page 8, first paragraph of applicant's remarks, applicant argues that "the Office Action has provided no reasoning nor evidence to suggest that the molecular interaction sites identified in, for example, histone, vimentin, ornithine decarboxylase, interleukin-2, or interleukin-4 mRNA cannot serve as a binding site for at least one molecule that when bound to the molecular interaction site modulates the expression of the RNA. Indeed, each of these molecular interaction sites contains ample secondary structure to serves as binding sites for other molecules. No evidence to the contrary has been presented in the Office Action. Further, any assertion by the Patent Office that an enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts so expressed".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, the specification defines "Modulation" as "augmenting or diminishing RNA activity or expression" (see the specification filed on May 12, 1999, page 10, last paragraph or the specification filed on October 21, 2002, page 6, lines 12-15). Although the specification adequately describes 3' untranslated regions of histone and vimentin mRNAs and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4, the specification does not adequately describe that a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 can be considered as a molecular interaction site since there is no evidence to show that binding of a molecule to a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4

can modulate (augment or diminish RNA activity or expression) the expression of said RNAs in said organisms. Second, although the examiner does not provide evidence to show that binding of a molecule to a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 cannot modulate (augment or diminish RNA activity or expression) the expression of said RNAs in said organisms, there is no evidence in available references to show that binding of a molecule to a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 can modulate (augment or diminish RNA activity or expression) the expression of said RNAs in said organisms. Furthermore, applicant does not provide evidence to show that binding of a molecule to a region selected from 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 can modulate (augment or diminish RNA activity or expression) the expression of said RNAs in said organisms. Third, although 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 contain ample second structures, this does not mean that these ample second structures can be considered as a molecular interaction site since there is no evidence to show that these ample second structures on 3' untranslated regions of histone and vimentin mRNA, and 5' and 3' untranslated regions of mRNAs from ornithine decarboxylase, interleukin-2 and interleukin-4 can modulate (augment or diminish RNA activity or expression) the expression of said RNAs in said organisms.

II. In page 8, second paragraph of applicant's remarks, applicant argues that because Applicants' recited method is supported by ample written description, product-by-process claims 35-41 and 43-67 are sufficiently described to show that Applicants' were, in fact, in possession of that which is claimed".

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection because, even though product-by process claims are limited by and defined by the process, the determination of the patentability of the product is based on the product itself. The patentability of a product does not depend on its method of production. *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). The method recited in claims 35-41 and 43-67 does not change structural limitations of claimed products recited in claims 35-41 and 43-67.

III. In page 9, first paragraph of applicant's remarks, applicant argues that "[R]eferring to claim 27, for example, the claimed oligonucleotide comprises a molecular interaction site. The specification is replete with the underlying characteristics of a molecular interaction site. Another recited identifying characteristic is that the molecular interaction site is present in prokaryotic RNA. Another recited identifying characteristic is that the molecular interaction site is present in at least one additional prokaryotic RNA. In addition, another recited identifying characteristic is that the molecular interaction site serves as a binding site for at least one molecule that when bound to the molecular interaction site modulates the expression of the prokaryotic RNA. These recited identifying characteristics are sufficient to show that Applicants were in possession of the claimed genus. The Office Action fails to provide any reasoning or evidence to support the position that such identifying characteristics are in any way inadequate".

This argument has been fully considered but it is not persuasive toward the withdrawal of the rejection. First, although applicant argues that "[T]he specification is replete with the underlying characteristics of a molecular interaction site", the specification does not provide a molecular interaction site that is present in prokaryotic RNA and in at least one additional prokaryotic RNA as recited in claim 27. Furthermore, applicant does not provide an evidence to support his position. Second, according to the definition of "Modulation" (see the specification filed on May 12, 1999, page 10, last paragraph or the specification filed on October 21, 2002, page 6, lines 12-15), an binding site of a molecule on a prokaryotic RNA can not considered as a molecular binding site as recited in claim 27. Only a binding site of a molecule on a prokaryotic RNA that can augment or diminish said RNA activity or expression can considered as a molecular interaction site recited in claim 27. However, the specification fails to provide such disclosure.

7. Claims 27-29 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the

prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to show that binding of one molecule to a molecular interaction site of a prokaryotic RNA can modulate the expression of said prokaryotic RNA but cannot modulate translation of said RNA. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability why binding of one molecule to a molecular interaction site of a prokaryotic RNA, which can modulate the expression of said prokaryotic RNA, cannot modulate translation of said RNA.

Claims 27-29 are directed to an oligonucleotide comprising a molecular interaction site that is present in prokaryotic RNA and in at least one additional prokaryotic RNA, wherein said molecular interaction site serves as a binding site for at least one molecule, wherein binding of said molecule to said molecular interaction site modulates the expression of said prokaryotic RNA and wherein the binding of said molecule to said molecular interaction site does not modulate translation of said RNA. The specification does not provide a guidance to show that binding of one molecule to a molecular interaction site of a prokaryotic RNA can modulate the expression of said prokaryotic RNA but cannot modulate translation of said RNA. Since it is known in the art that DNA transcripts to RNA and then the RNA translate to protein (see TEXTBOOK of Biochemistry with clinical correlations, Third Edition, 1992, pages 622), a factor that affects a RNA expression must affect the RNA translation. In view if claims 27-29,

it is unclear why binding of one molecule to a molecular interaction site of a prokaryotic RNA, which can modulate the expression of said prokaryotic RNA, cannot modulate translation of said RNA.

With above unpredictable factor, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether there is a molecular interaction site of a prokaryotic RNA that can modulate the expression of said prokaryotic RNA but cannot modulate translation of said RNA.

Response to Arguments

In page 9, third paragraph bridging to page 10, second paragraph of applicant's remarks, applicant argues that "[C]laim 27, however, does not recite that the binding of a molecule to a molecular interaction site 'only' can modulate the expression of the prokaryotic RNA while not modulating translation of the RNA. The only functional language recited in claim 27 is that the 'molecular interaction site serves as a binding site for at least one molecule that when bound to said molecular interaction site modulates the expression of said prokaryotic RNA' and that 'the binding of said molecule to said molecular interaction site does not modulate translation of said RNA.' One skilled in the art desiring to determine whether: 1) a 'molecular interaction site serves as a binding site for at least one molecule that when bound to said molecular interaction site modulates the expression of said prokaryotic RNA'; and 2) 'the binding of said molecule to said molecular interaction site does not modulate translation of said RNA' need only perform routine experimentation. Nowhere does the Office Action suggest, let alone support with evidence, that such testing is anything but routine. Indeed, RNA expression assays and RNA

translation assays have been widely known to and used by the skilled artisan for years. Further, experiments to determine the rate of transcription, RNA maturation, RNA transport, and intracellular RNA localization, each of which can modulate the expression of the prokaryotic RNA".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection. First, the examiner agrees with applicant that claim does not recite that the binding of a molecule to a molecular interaction site only can modulate the expression of the prokaryotic RNA, the word "only" has been removed from the rejection. However, the word "only" in the office action does not affect the rejection. Second, since it is known in the art that DNA transcripts to RNA and then the RNA translate to protein (see TEXTBOOK of Biochemistry with clinical correlations, Third Edition, 1992, pages 622), a factor that affects a RNA expression must affect the RNA translation. Although "RNA expression assays and RNA translation assays have been widely known to and used by the skilled artisan for years. Further, experiments to determine the rate of transcription, RNA maturation, RNA transport, and intracellular RNA localization, each of which can modulate the expression of the prokaryotic RNA", the specification does not provide a molecular interaction site of a prokaryotic RNA that can modulate the expression of said prokaryotic RNA and can not modulate translation of said RNA. Therefore, it is concluded that undue experimentation is required to make the invention as it is claimed. The undue experimentation at least includes to test whether there is a molecular interaction site of a prokaryotic RNA that can modulate the expression of said prokaryotic RNA but cannot modulate translation of said RNA.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 35-40, 43-57, and 59-67 are rejected under 35 U.S.C. 102(b) as being anticipated by Molecular Biology of The Cell, Third Edition (pages 466, 1994).

Regarding claims 35, 39, 40, 51, 52, 56, 57, and 67, since Molecular Biology of The Cell, Third Edition teach poly-A-binding proteins and it is known that mRNA from eukaryotic cells has a polyA tail that can affect mRNA stability (ie., modulating the expression of mRNA) (see page 466), polyA tail is a molecular interaction site as recited in claims 35, 39, 40, 51, and 52, 56, 57, and 67. Although the molecular interaction site taught by Molecular Biology of The Cell, Third Edition is not identified by the method recited in claims 35, 51, 52, and 67, it is well established that even though product-by process claims are limited by and defined by the process, the determination of the patentability of the product is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product is made by a different process. *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Regarding claims 36-38, 43-50, 53-55, and 59-66, since these claims are product-by process claims and are dependent on claims 35 and 52, they are also rejected.

Therefore, Molecular Biology of The Cell, Third Edition teaches all limitations recited in claims 35-40, 43-57, and 59-67.

Response to Arguments

In page 4, third paragraph bridging to page 5, first paragraph of applicant's remarks, applicant argues that "[E]ach of the rejected independent claims recites an 'oligonucleotide comprising a molecular interaction site...' (emphasis added). Page 466 of the Molecular Biology reference does not teach any oligonucleotide, let alone an oligonucleotide that comprises a molecular interaction site. Rather, the nucleic acid molecule that contains the polyA tail depicted on page 466 of the Molecular Biology reference is an mRNA. An mRNA molecule is not an Oligonucleotide".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection because a mRNA molecule can be considered as an oligonucleotide since the claims do not limit the size of the claimed oligonucleotide. Furthermore, applicant does not indicate why a mRNA molecule is not a claimed oligonucleotide.

10. Claims 27, 35-38, 41, 43-55, and 58-67 are rejected under 35 U.S.C. 102(b) as being anticipated by Zubay (Biochemistry, third edition, pages 817 and 818, 1993).

Regarding claims 27, 35, 41, 51, 52, 58, and 67, since Zubay teaches that RNase P binds to tRNA and specially cuts 5' to tRNA-like structure in E. Coli (see pages 817 and 818), tRNA has a molecular interaction site for RNase P as recited in claims 27, 35, 41, 51, and 52, 58, and 67 because RNase P modulates the expression of tRNA by cutting tRNA. Although the molecular interaction site taught by Zubay is not identified by the method recited in claims 35,

51, 52, and 67, it is well established that even though product-by process claims are limited by and defined by the process, the determination of the patentability of the product is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product is made by a different process. *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985).

Regarding claims 36-38, 43-50, 53-55, and 59-66, since these claims are product-by process claims and are dependent on claims 35 and 52, they are also rejected.

Therefore, Zubay teaches all limitations recited in claims 27, 35-38, 41, 43-55, and 58-67.

Response to Arguments

In page 5, second paragraph to fourth paragraph of applicant's remarks, applicant argues that "[E]ach of the rejected independent claims recites an 'oligonucleotide comprising a molecular interaction site. . .' (emphasis added). Page 818 of the Biochemistry reference does not teach any oligonucleotide, let alone an oligonucleotide that comprises a molecular interaction site. Rather, the nucleic acid molecule that contains the RNase P binding site is an entire tRNA molecule. An entire tRNA molecule is not an oligonucleotide. Indeed, the molecular interaction sites which is present within the claimed oligonucleotides is present in the RNA of a selected organism. Although the RNA that is within the selected organism can be a tRNA, the oligonucleotide is not a tRNA molecule".

These arguments have been fully considered but they are not persuasive toward the withdrawal of the rejection because a tRNA molecule can be considered as an oligonucleotide

since the claims do not limit the size of the claimed oligonucleotide. Furthermore, applicant does not indicate why a tRNA molecule is not an oligonucleotide.

Conclusion

11. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

12. No claim is allowed.

13. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (571)272-0745.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
November 30, 2004

KENNETH R. HORLICK, PH.D
PRIMARY EXAMINER
12/2/04